Ethical Allocation Framework for Bamlanivimab and the Combination Casirivimab/Imdevimab Treatment of Covid-19 in Wisconsin

Background

The purpose of this document is to develop a fair and equitable framework for the allocation of scarce emerging treatments for Covid-19, with specific focus on the monoclonal antibodies bamlanivimab and casirivimab/imdevimab, which have both been issued Emergency Use Authorization (EUA) by the US FDA). Allocation of these medications to the states has been determined by the FDA based on confirmed hospitalizations and confirmed cases (7-day averages). These drugs are monoclonal antibodies that target the spike protein of coronavirus-SARS-V2, the virus that causes Covid-19. Once bound, they prevent the virus from entering human cells. Ongoing studies suggest that these may be effective in reducing viral load, symptoms, and the risk of hospitalization in patients recently diagnosed with mild to moderate Covid-19[1,2].

A committee process to determine ethical allocation frameworks is recommended by the U.S. Department of Health and Human Services. This framework has been developed by a therapeutics allocation sub-committee of the Wisconsin State Disaster Medical Advisory Committee (SDMAC), and is based upon a foundational ethical framework already developed and adopted by the SDMAC. The Therapeutics Allocation Subcommittee consists of physicians trained in critical care, infectious disease, pediatrics, and internal medicine; hospital pharmacists, and experts in allocation frameworks and ethics. The following criteria and instructions can be found in the EUA and their accompanying Fact Sheets.

The framework below is based on the best information available at the time of writing. It will be updated to reflect changes in the availability of drugs, evidence of efficacy, and learned experience.

Eligiblity to Receive Bamlanivimab or Casirivimab/Imdevimab:

- Patients must have one or more mild to moderate symptoms of COVID-19 and positive results of direct SARS-CoV-2 viral testing (PCR or rapid antigen testing is acceptable).
- Patients must be 12 years of age and older, weighing at least 40 kilograms (about 88 pounds).
- Patients must be **at high-risk of complications** from a Covid-19 infection. High risk (as defined by the current EUA) is a patient who meets at least one of the following criteria:
    - Age ≥65 years
    - Body Mass Index (BMI) ≥35
    - Chronic Kidney Disease
    - Diabetes
    - Immunosuppressive disease
    - Receiving immunosuppressive therapy
    - Are ≥55 years of age AND have

        - cardiovascular disease, OR
        - hypertension, OR
        - chronic obstructive pulmonary disease/other chronic respiratory disease.
    - Are 12–17 years of age AND have
        - BMI ≥ 85th percentile for their age and gender based on CDC growth charts, https://www.cdc.gov/growthcharts/clinical_charts.htm, OR
        - sickle cell disease, OR
        - congenital or acquired heart disease, OR
        - neurodevelopmental disorders, for example, cerebral palsy, OR
        - a medical-related technological dependence (tracheostomy, gastrostomy, or positive pressure ventilation not related to COVID-19), OR
        - asthma, reactive airway or other chronic respiratory disease that requires daily medication for control.

- These monoclonal antibodies may only be administered in settings in which health care providers have immediate access to medications to treat a severe infusion reaction, such as anaphylaxis, and the ability to activate the emergency medical system (EMS), as necessary.
- Bamlanivimab or Casirivimab/Imdevimab should be given as soon as possible after a positive direct SARS-CoV-2 viral test and within 10 days of symptom onset.

Bamlanivimab and Casirivimab/Imdevimab are not authorized for use in the following patient populations:

- Adults or pediatric patients who are hospitalized due to Covid-19.
- Adults or pediatric patients who require oxygen therapy due to Covid-19.
- Adults or pediatric patients who require an increase in baseline oxygen flow rate due to COVID-19 in those patients on chronic oxygen therapy due to underlying non-COVID-19-related comorbidity.

Underlying Principles to Guide Equitable Vaccine and Therapeutics Allocation

Please refer to Ethics Subcommittee Ethical Framework to Guide the Allocation of COVID-19 Therapeutics and Vaccines for a review of underlying principles influencing this document.

Ethical Justification for Proactively Mitigating Health Disparities in Covid-19 Outcomes

COVID-19 has had a disproportionate impact on low income communities and certain racial/ ethnic minorities in the United States. Equity calls attention to the systematic differences in health outcomes and opportunities to be healthy that adversely affect socially discounted and/or marginalized groups. For Covid-19, these inequities may arise from higher burdens of pre-

existing comorbid disease, poor health care access, or not having the option for social distancing due to living in densely-populated neighborhoods or households. There are also more economically disadvantaged individuals working essential jobs during the pandemic, and many are unable to perform job functions from the safety of their home. This puts them at greater risk of interacting with others who may transmit Covid-19. Public health interventions may be used to attempt to mitigate these disparities in Covid-19 by recognizing the structural inequities that underlie them. One way to do this is to account for a level of social vulnerability in the allocation guidelines used by the state to alleviate disease burden, such as novel therapeutics. The CDC's Social Vulnerability Index (SVI) is one measure that uses 15 US census variables (such as poverty and crowded housing) to measure a community's resilience to stressors, including disasters like the Covid-19 pandemic (https://www.atsdr.cdc.gov/placeandhealth/svi/at-a-glance_svi.html). SVI has been used by other states, such as Pennsylvania, in their therapeutic allocation protocols. It is preferred over other measures like the Area Deprivation Index (ADI) due to its increased number of variables included. Considering SVI may increase the allocation of a scarce resource to areas most heavily impacted by **both** Covid-19 and structural inequities, recognizing that those inequities may independently increase the risk of poor outcomes from Covid-19.

Allocation of Bamlanivimab and Casirivimab/Imdevimab to Healthcare Facilities

The Wisconsin Department of Health soon expects to receive initial disbursements of limited quantities of the monoclonal antibodies from the federal government. The intention of federal disbursement is to ensure the most fair and equitable allocation of a medication that is currently of limited availability. Wisconsin will continue to receive the medication in this form until the situation of scarcity is no longer a concern and the drug can be purchased freely by health systems.

Multiple phases of disbursement are intended, but for the initial disbursement phase, bamlanivimab and/or casirivimab/imdevimab may only be allocated to the health systems already receiving the FDA approved antiviral medication, remdesivir. These drugs must be administered intravenously in normal saline, infused over the course of one hour, and require monitoring of the patient for a minimum of one-hour post-infusion for any signs/symptoms of allergic reaction. Disbursement of the medication to hospitals and health systems already receiving and administering intravenous Covid-19 medication ensures adequate infrastructure and staff support for the complex administration of the medication.

For the initial phase of drug distribution from the federal government, the amount of bamlanivimab and casirivimab/imdevimab allocated to each hospital or health system will be determined by the Wisconsin Department of Health Services based upon county-level data regularly collected on confirmed Covid-19 cases by age. The drugs will be distributed directly from the supplier, and divided proportionally among the hospital(s)/site(s) within a county that are equipped to administer it.

Psychiatric hospitals and surgical centers are not eligible to receive the drug.

The framework for the state allocation of bamlanivimab and casirivimab/imdevimab consists of three main steps:

1) Determine the proportion of doses allocated based on county level data.

Allocation is based on county Covid-19 burden (number of cases among individuals ≥ 65 years in past 7 days) AND county Social Vulnerability Index (SVI). Rather than allocate proportionally based on raw case counts across counties, the state will adjust each county's case count to reflect the background social vulnerabilities of residents in each county. Counties are divided into four quartiles based upon SVI, and case counts are weighted appropriately by quartile.

- Case counts in the 1st quartile SVI counties (highest SVI counties, most disadvantaged) will be increased by 25% before determining their proportional allocation.
- Case counts in 2nd quartile SVI counties will be increased by 12.5%.
- Case counts in 3rd quartile SVI counties will be increased by 6.25%.
- Case counts in 4th quartile SVI counties will not be altered prior to determining proportional allocation.

2) Distribute drugs to hospitals/health systems based on total proportion calculated in step 1.

- For counties with only one hospital, the entire allocation will go to that hospital.
- For counties with more than one hospital, treatment courses will be allocated proportionally based on the average daily Covid-19 hospital admissions through the hospital's Emergency Department (ED) over the past 7-days.
- For counties without hospitals, the allocation will be made to a neighboring county where residents can receive the drug based on input from that county's public health officials.
- For health systems that serve multiple counties, they will receive the total number of treatment courses from all counties served.
- If a hospital opts out, the drug will be reallocated among other sites within that county according to methodology explained above.

Bamlanivimab and casirivimab/imdevimab will be distributed with the intent that they are to be used to serve local communities. To promote access, hospitals/health systems are allowed to move the drugs between sites of care in order to maximize benefit to patients and best serve the common good by alleviating stress on health care resources.

3) Hospitals follow EUA eligibility criteria to develop a process of allocation to individual patients based on ethical principles.

The Wisconsin DHS has developed an initial framework for the allocation of bamlanivimab and casirivimab/imdevimab to hospitals and health systems, but these systems must develop their own treatment protocols for individual patients consistent with the ethical principles outlined in the accompanying "Principles" document.

In general, treating clinicians should not be responsible for operationalizing the allocation framework. This should be led, instead, by crisis triage officers or clinic leaders. The principle of "fairness," as outlined in the Ethics Subcommittee Ethical Framework to Guide the Allocation of

COVID-19 Therapeutics and Vaccines requires that healthcare resources be allocated using criteria based **only on relevant characteristics**, using impartial procedures for allocation and distribution. This means that the team making allocation decisions should be blinded to information that is not relevant. As stated in the Ethics Subcommittee document, the following considerations should not be used to unjustly disadvantage individuals in allocation decisions, in no particular order: age, race, color, disability, gender, immigration/citizenship status, incarceration status, national origin, religion, sexual orientation and gender identity, socioeconomic status and ability to pay. Methods that should generally be avoided include "first-come, first-served" or random lottery of all Covid-19 patients. These strategies do not preserve resources to maximize the common good and may exacerbate existing health disparities.

We recommend that ethics committee representation and crisis triage teams be involved in determining a process for allocation that is equitable, fair, and reasonable.

Topics for ethics committee and crisis triage teams to <u>consider</u> in the development of hospital/health system level allocation frameworks:

- Use of additional clinical criteria for treatment eligibility beyond those specified in the EUA, in order to maximize benefit, for example:
    - Prioritizing persons who have a higher number of qualifying comorbidities.
    - Prioritizing older adults in congregate/overcrowded living situations.
- Patient care responsibility for patients tested outside the hospital/health system
    - Health systems that participate in community testing supported by the state should include all those tested as possible recipients of allocation if they meet criteria
- Evaluation of a lottery system. After risk-based criteria and ethical principles are applied and there are still not enough resources for each person who meets the criteria, lotteries can be ethically appropriate strategies to use in decision making. In this way, lotteries allow for each eligible patient to have an equitable chance of receiving the drug. One approach is to randomly allocate among eligible patients. Another is to weight the lottery based on relevant factors in order to advance fairness and health equity.

For an example of a policy that aligns with the ethical allocation goals outlined in this document and makes use of a weighted lottery, please refer to **Appendix A**. This is one example from the state of Pennsylvania, but there are many other possible methods that meet ethical goals stated here.

The following are member of the Therapeutics Allocation Sub-Committee of the SDMAC who provided valuable expertise for the creation of this framework:

<u>Committee Members</u>

Alyson Capp, PhD (co-chair)
Director of Ethics
Advocate Aurora Health

Sarah Sorum, PharmD (co-chair)
Executive Vice President & CEO
Pharmacy Society of Wisconsin

Dennis Brierton, Pharm D, BCPS, FASHP
System Director, Clinical Pharmacy
Advocate Aurora Health

Gina Dennik-Champion, MSN, RN, MSHA
Executive Director
Wisconsin Nursing Association

Helen Marks Dicks, JD
State Issues Advocacy Director
AARP Wisconsin

J. Paul Kelleher, PhD
Associate Professor
UW-Madison

Mohammad (Mo) Kharbat - MBA, BPharm, R.Ph., BCPS
Regional VP of Pharmacy Services
SSM Health

Elizabeth (Liz) Laubach, PharmD, BCPS
Regional Director of Pharmacy
Ascension Wisconsin

Steven R Leuthner, MD, MA
Neonatal-Perinatal Medicine and Center for Bioethics
MCW & Children's Wisconsin

Eric Marty, MD
Director of Palliative Care
Agrace

Sridevi Mohan, MPH, MA
Epidemiologist
Public Health Madison & Dane County

Carlo Nevicosi, APSW
Deputy Director
Walworth County Health & Human Services

J. Njeri Wainaina, MD, FACP
Associate Professor of Medicine and Surgery
Medical College of Wisconsin

Staff
Margaret Nolan, MD, MS
Physician-Scientist
UW-Madison

Preston Leavitt
Program Support

References

1) News Release. **“**Lilly announces agreement with U.S. government to supply 300,000 vials of investigational neutralizing antibody bamlanivimab (LY-CoV555) in an effort to fight COVID-19.” October 28, 2020.
2) FDA News Release. “Coronavirus Update: FDA Authorizes Monoclonal Antibodies for Treatment of Covid-19. November 21, 2020.” https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-authorizes-monoclonal-antibodies-treatment-covid-19